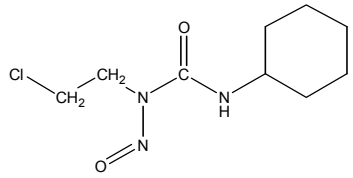
1-(2-CHLOROETHYL)-3-CYCLOHEXYL-1-NITROSOUREA
CAS No. 13010-47-4
First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.26, 1981; IARC S.4, 1982; IARC S.7, 1987). When administered by intraperitoneal or intravenous injection, 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea induced lung carcinomas in rats of both sexes. When the compound was administered by intraperitoneal injection, an increase in the incidence of lymphosarcomas was reported in mice of both sexes (IARC V.26, 1981; IARC S.4, 1982; IARC S.7, 1987). Application of the compound to the skin of mice did not induce skin tumors, but the duration of the experiment was considered inadequate for the results of this study to be relevant (IARC V.26, 1981; IARC S.7, 1987).

There are no adequate data available to evaluate the carcinogenicity of 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea in humans (IARC S.4, 1982). In several reported cases, cancer patients who received the compound developed leukemia. With one exception, all of these patients had also received other cytotoxic agents and/or irradiation (IARC S.4, 1982; IARC V.26, 1981).

PROPERTIES

1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea is a yellow powder that is soluble in 10% ethanol and absolute ethanol and is slightly soluble in water. The compound is sensitive to both oxidation and hydrolysis and forms alkylating and carbamoylating intermediates. When heated to decomposition, it emits very toxic fumes of hydrochloric acid and other chlorinated compounds as well as nitrogen oxides (NO_x).

USE

1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea is an antineoplastic agent. The compound has had limited use since the early 1970s in the treatment of Hodgkin's disease and various solid tumors, such as primary and metastatic brain tumors, where it is given alone or in combination; for colorectal tumors, where it is given in association with 5-fluorouracil; and for certain pulmonary malignancies. It is usually used in conjunction with other antineoplastic drugs (IARC V.26, 1981).

PRODUCTION

Current production, import, and export data on 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea are not available. The compound was believed to be produced by one U.S. company in 1981, but no production volumes were reported (IARC V.26, 1981; SRIa, 1986). 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea was first synthesized in the United States in 1966 (IARC V.26, 1981).

EXPOSURE

The primary routes of potential human exposure to 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea are inhalation, dermal contact, and ingestion. Patients are exposed to the compound when it is used as an antineoplastic agent. The recommended dose for adults and children is 130 mg/m^2 body surface, given as a single dose every 6 weeks (IARC V.26, 1981). Potential occupational exposure may occur during the production, formulation, packaging, and administration of the pharmaceuticals. No estimate has been made on the number of potential exposures to 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea.

REGULATIONS

This chemical is used as a pharmaceutical, and in low quantities relative to other chemicals; therefore, it is of little regulatory concern to EPA. However, there may be a small pollution problem relative to hospital wastes. FDA regulates 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea under the Food, Drug, and Cosmetic Act (FD&CA) as a prescription drug approved for human use. FDA also requires warning labels on this drug concerning its potential carcinogenicity, mutagenicity, teratogenicity, and/or impairment of fertility. OSHA regulates this drug under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-21.